Foreword

Striving to understand nature provided the impetus for much of our philosophical ideas, scientific discoveries, and technological advances whose beneficial results we came to enjoy as a species throughout history. Understanding the molecules of life—nucleic acids, proteins, and secondary metabolites, commonly referred to by organic chemists as natural products—is arguably one of the most important human endeavors, one in which the benefits reaped by science and society are both immense and undisputed. Indeed, the emergence of the structure of the molecule and the art of its synthesis in the nineteenth century set the stage for the development of all of organic chemistry and biochemistry and much of modern biology and medicine. Natural products played a protagonist role in these developments. Their isolation, structural elucidation, and synthesis challenged and stimulated analytical and purification techniques and instrumentation, method development, and synthetic strategy design. Today, because of the enormous advances made over the last two centuries in the chemistry, biology, and medicine of natural products, people around the world enjoy untold benefits with regard to healthcare, nutrition, cosmetics, and fashion, just to name a few areas.

I was honored by the invitation of Professors Sunil and Bani Talapatra to provide a Foreword to their book and enjoyed reading various versions of their prepublication manuscripts. Much to my delight, I found them to be stunningly illuminating in terms of breadth and depth of coverage of essentially the entire field of chemistry, biology, and medicine of plant-derived natural products. Their accomplishment in putting together this tome is beyond the normal boundaries of most books written on the subject, and they deserve our admiration and respect for bringing together the various aspects of this important field.

In the chapters that follow, the authors focus on the molecules of life, particularly those natural products derived from plants, dwelling on such wide ranging aspects as enzymatic transformations, biosynthetic pathways, isolation, and structural elucidation (including techniques and instrumentation), conformation, total synthesis, biological activities and functions, symbiotic relationships, medical applications, biochemistry, and stereochemistry. The latter topic is discussed in considerable detail and its impact on the chemical and biological properties of the
molecule and its asymmetric synthesis are articulated and explained. The special emphasis on conformation is particularly informative and educational and provides useful insights and understanding of the nature of the molecule to students of organic chemistry. The various aspects of the science of natural products are elaborated upon by using selected natural product classes and individual compounds, such as terpenoids and alkaloids, to underscore the influential impact of these endeavors in advancing the discipline of organic chemistry, including theory, experimental methods and techniques, chemical synthesis, biology, medicine, and nutrition.

Three appendices at the end of the book provide interesting and useful biographical information on selected pioneers, major discoveries and inventions, and extra educational material for learning. Indeed, this opus is intended as both a reference book and a teaching text where one can find important facts, inspiration, and pedagogy. The structure of the book allows for easy selection of separate topics for reading and teaching. Congratulations and many thanks to Professors Sunil and Bani Talapatra for an outstanding treatise which will remain a classic in the field and hopefully serve to maintain its momentum and proliferation with new admirers, recruits, and supporters.

Houston, TX

K.C. Nicolaou
Preface

Linus Pauling [NL 1954 (Chemistry), 1962 (Peace)] once said “A good book or a speech should be like a Lady’s dress. It should be long enough to cover the essentials and short enough to reveal the vital statistics.”

With this caveat in mind, it becomes a challenging task to author an adequately balanced textbook which shall capture the essentials and address the leading frontiers, while staying focused within the broader scope of the subject area. During our long postgraduate-level teaching career spanning more than three decades, we felt the unmet need of a textbook on Plant Natural Products, the Secondary Metabolites, that covered the fundamental aspects of the relevant chemistry, stereochemistry, biosynthesis, and bioactivity in sufficient depth, elaborated using well-known representative members.

Here we have made an attempt to write a book intended to serve as a textbook for advanced undergraduate and graduate/postgraduate students as well as a reference guide for researchers and practicing organic and pharmaceutical chemists who may wish to gain a better understanding of various aspects of the chemistry of natural products. It is almost an impossible task to write a comprehensive textbook dealing with all facets of natural products chemistry of even some of the selected classes of molecules due to the rapidly expanding literature in this area. Hence, we have deliberately not roamed too far to make this a comprehensive textbook, but rather tried to create one that will provide sufficient background in the general area of natural products chemistry and serve as an adequate launching pad for an in-depth and specialized investigation.

This book grew primarily out of our 68 years of combined postgraduate teaching experience in natural products chemistry and stereochemistry at the Calcutta University and at some other universities. We have limited our discussions to some well-studied natural products of plant origin, which have contributed significantly to the advancement of organic chemistry. The choice from the endless variations of natural products is entirely personal, driven by our perception of model natural products for our target readers. Our coverage of the material is illustrative of the vastness, diversification, and continued growth of this particular area of chemistry.
The distinguishing feature of this book is the discussion on the stereochemical aspects, the hallmark of chiral natural products, and the inclusion of a chapter exclusively dedicated to stereochemistry (Chap. 2). This chapter will be helpful in understanding various updated nomenclatures, stereostructures, asymmetric synthesis, biosynthesis, and bioactivities (chiral recognition in vivo) of natural products that appear in subsequent chapters. Furthermore, wherever possible, we have given plausible mechanistic rationalizations of product formations which are less obvious, during the portrayal of reactions and synthesis of natural products. Original literature has been referenced, with titles of the articles (with the exception of titles of some very old references, which could not be procured), to give interested readers an idea of the subject matter contained in such articles.

Chapter 1 offers a preliminary introduction to enzymes, coenzymes, and primary and secondary metabolites (natural products), illustrates various biological functions of the metabolites, and summarizes the identified metabolic pathways leading to the different types of natural products.

Chapter 3 deals with few important biochemical events related to the discussions in the subsequent chapters on the biogenesis and biosynthesis of major skeletal patterns formed sometime during three billion years of evolution.

Various synthetic methodologies, separation techniques, and instrumental analysis have been invented and developed in connection with the natural products chemistry research. In Chap. 4, we have discussed some widely used isolation procedures and separation techniques (Sect. 4.1). The chapter also touches upon traditional and state-of-the-art methods for structural elucidation of naturally occurring molecules (Sect. 4.2).

During the discussions on the “Biosynthesis of Terpenoids: the oldest Natural Products” (Chap. 5) or on the biosynthesis of other natural products (other Chapters), no extensive description of the enzymes and their processes has been provided. The biosynthetic conversions are explained in terms of the currently accepted mechanisms of organic reactions, with special attention to the stereochemical features of the processes.

Mother Nature uses organic molecules as the building blocks for the natural product framework. Barton (NL 1969) said, “if we assume that enzymatically-induced reactions follow the same mechanistic principles as ordinary organic reactions we can at least make an approach to the subject” [1]. Likewise, R. Kluger wrote in an article [2] “It is useful if the reactions can be systematically divided into mechanistic types (such as Ingold formulation [Ingold, 1953]. The most common examples of this type of classifications are the two general nucleophilic substitution mechanisms, \( S_N1 \) and \( S_N2 \).” The synthetic methodologies used by Nature are amazingly simple, as exemplified by aldol, acyloin, and Claisen condensations, olefin-cation addition/cyclization, Markonikov additions, simple \( S_N1 \), \( S_N2 \), \( S_N2' \), E1, and E2 reactions, and 1,2-trans migrations for creating carbon–carbon bonds—the life string of organic molecules. Nature’s substrates for the biosynthesis of complex natural products are also simple (e.g., small carbonyl compounds, L-amino acids, olefins, etc.).
Chapters 6–29, including a number of sections (sub-chapters) of Chaps. 6–8, 10, 13, and 14, deal with the chemistry of individual compounds classified according to the major biogenetic pathways. Many basic concepts and ideas have been discussed. Though the tone of discussions on natural products has changed during the last few decades, we have given adequate attention to the work of past great chemists in dealing with the individual compounds, because we believe that their work will never go out of date; rather it will exist to impart the spirit of enquiry and forms the foundation to our current understanding. In this context we quote from the abstract of Barton’s talk entitled “Oxygen and I” in the 10th Johnson Symposium 1995 held at Stanford University: “In Chemical Sciences, the distant past, the near past and the present join together in continuous harmony…. The lecture will illustrate how past chemistry should not be forgotten.”

Chapter 15 is a general introduction to alkaloids. Chapters 16–29 include detailed discussions on some well-known alkaloids derived from various biogenetic precursors. Chapter 30 contains structures with relevant references of a number of alkaloids of diverse skeletal patterns (not discussed due to space constraint).

Important concepts such as conformational analysis, stereochemistry, biomimetic synthesis, retrosynthetic approach, pericyclic reactions, Fischer and Newman projection formulas, and many organic reactions owe their genesis and/or refinement to the natural products chemistry. With his understanding of squalene-2,3S-oxide (a natural product), the phenomenon of catalysis, and his passion for the transition metals of the Periodic Table, “the most elegant organizational chart ever devised” [3], Sharpless (NL 2001) invented Sharpless epoxidation—a near chemical substitute for an enzymatic reaction. The trisubstituted olefinic alcohol, geraniol, a natural product with an attractive smell that was a great favorite of Sharpless [4], was used by him to successfully implement the most challenging asymmetric epoxidation and dihydroxylation. Chapter 31 attempts to bring together such important outcomes of natural products chemistry research.

The contribution of natural products in asymmetric synthesis is immense. Natural chiral auxiliaries take the place of enzymes in some chemical reactions, and the chemical literature is flooded with reports on such chiral auxiliaries. Chapter 32 has been dedicated to chiral recognition in biological systems and the use of natural products and their derivatives as chiral auxiliaries. This chapter illustrates the differences in biological properties exhibited by each component in a pair of stereochemically nonequivalent enantiomeric twins, i.e., enantiomeric stereoselectivity.

The medicinal values of many natural products are now evaluated scientifically to give them the drug status. Further, many of them served as the lead molecules for the synthesis of cost-effective therapeutic molecules with promising medicinal values. This is one of the important value-added dimensions of natural products chemistry. Chapter 33 deals with *The Natural Products in the Parlor of the Pharmaceuticals*. Chapter 34, entitled *Organic Phytonutrients, Vitamins and Antioxidants*, presents the multitude of useful biological functions of nutraceuticals, as well as natural products that are consumed daily through diet in the form of spices,
vegetables, fruits, and drinks. This chapter may also stimulate interest of the uninitiated readers.

Carbohydrates form a very important class of bioorganic molecules whose chemical and biochemical properties revolve around their stereochemical and conformational features. The chemistry of carbohydrates has grown enormously during the last few decades and involves their use as templates in the synthesis of complex chiral natural products. However, since their biosynthesis and biodegradation are routed through primary metabolic/catabolic pathways, they are referred to as primary metabolites according to conservative definition and do not fall within the scope of secondary metabolites and hence have not been included.

Brief biographical sketches of 31 pioneering chemists, who we believe immensely enriched the realm of natural products chemistry, appear in Appendix A. We hope that these great personalities will inspire the young readers and motivate them in their professional pursuits. In the absence of space constraint, several more such life sketches could have been included, since concepts and ideas often develop through the collaborative and collective intellectual engagement and may not be attributed to a single discoverer. We sincerely regret our inability to be all-inclusive in this regard.

Appendix B chronologically lists some landmark inventions/discoveries in the field of natural products which may be interesting and inspiring to readers.

Appendix C contains miscellaneous information geared towards students and some often-overlooked conventions. For convenience, a list of Abbreviations has been provided before the Table of Contents.

Both in the Preface and in the body of the text, we took the liberty of quoting from books, articles, lectures, and letters (original references provided wherever appropriate), in order to impart deeper insights and broader perspectives related to the topics discussed.

We hope that the present version of the text will be well adapted to the teaching of natural products chemistry at the senior undergraduate and graduate/postgraduate levels. Students should get a flavor of the subject and be able to comfortably move forward with more advanced topics both within the domain of natural products chemistry and beyond. The teachers with limited teaching time and resources should be able to pick and choose topics of interest to them, aligned with the level of the course they intend to offer.

Acknowledgments: Acknowledgments and thanks are not casual words—they have their origin in our hearts. The job of writing this book could not have been accomplished without the help of our supporters and well-wishers from various walks of life.

We express our deepest gratitude and heartfelt thanks to Professor K. C. Nicolaou first for kindly going through the Sect. 8.4 on Taxol® and then the whole of the first draft of the Chapters and Appendices, at our requests from time to time, for enriching them with helpful suggestions and valuable comments on the overall content, and finally for kindly writing the Foreword with his candid opinion, in spite of his heavy academic and administrative commitments.
Informational support received from Professors A. R. Battersby, C. Djerassi, K. Nakanishi, K. C. Nicolaou, and R. Noyori during drafting of their life sketches is acknowledged with deep gratitude. We are grateful to Professor Alex Nickon for his encouraging comments on Sect. 7.5 (on caryophyllene) and to Professor Sukh Dev for his encouragement in our endeavor. We are sincerely thankful to Dr. B. N. Roy (Lupin Limited, Pune) for several academic correspondences and constructive suggestions. Our affectionate thanks go to Dr. Sanchita Goswami [Calcutta University (CU)] for continual supply of PDF files of research papers needed as references for the last 3 years and to Mr. Debajyoti Saha [Indian Association for the Cultivation of Science (IACS), Kolkata] for the past 1 year.

The inputs received from our professional colleagues, friends, and former students during the preparation of the manuscripts have been extremely valuable. Special mention should be made of Dr. Bhupesh C. Das (CNRS, Gif-sur-Yvette, France), Professor Manoj K. Pal (SINP, Kolkata), Professor Amitabha Sarkar (IACS), Professors Anil K. Singh and S. Kotha (IIT Bombay), Professor Kankan Bhattacharyya (IACS), Professor Swadesh R. Roychaudhuri (Jadavpur University, Kolkata), Dr. Arun K. Shaw (CDRI, Lucknow), Dr. Debashis Samanta (CLRI, Chennai), Professor Asutosh Ghosh, and Dr. Dilip K. Maiti (CU), Dr. Rajyasri Ghosh (Scottish Church College, Kolkata), Mr. Nandadulal Biswas (Library, CU), Mr. Asoke Mukherjee (CU, College Street Campus), Mr. Amar Chand De (Sarat Book House, Kolkata), Mr. Harry Ridge (Sheffield), and Dr. Bimal R. Bhattacharyya (Market Harborough, England). The library facilities of the Calcutta University, IIT Bombay, IACS (Kolkata), and UC Berkeley are acknowledged with gratitude.

We are solely responsible for errors, inconsistencies, and infelicities that may persist in the text and Figures, despite our most sincere efforts to eliminate them. Our endeavors will be meaningful if the book benefits the target readers. We welcome any corrective suggestions and recommendations for the future edition of this book.

Kolkata, India

Sunil Kumar Talapatra <talapatrask@gmail.com>
July, 2013

Bani Talapatra <banitalapatra@yahoo.co.in>

References

Chemistry of Plant Natural Products
Stereochemistry, Conformation, Synthesis, Biology, and Medicine
Talapatra, S.K.; Talapatra, B.
2015, LXIII, 1180 p. 1015 illus., 21 illus. in color. In 2 volumes, not available separately. Hardcover
ISBN: 978-3-642-45409-7